GOLDSTEIN & HEALEY
L.L.P.
Attorneys at Law

1177 West Loop South, 10th Fl.
Houston, Texas 77027
713/877-1515
713/877-1737 (facsimile)

FACSIMILE COVER SHEET

DATE: February 14, 2002

TO: Robert Joynes

FACSIMILE: 703/746-5330

FROM: Dee Malone

PAGES TO FOLLOW: 24

MESSAGE:

Attached are the documents from the file histories that I was told to send to you. I hope it is what you were needing. Let me know if I can be of further assistance.

08/082,804 06/25/93

Continuation of 07/742,574 08/07/91

710. – 101

A/FWC

08 082804

#37/I

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

10/27/93

Docket No: 31510

FILE WRAPPER CONTINUING APPLICATION TRANSMITTAL UNDER 37 CFR 1.62

Box FWC
Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

This is a request under 37 CFR 1.62 for filing a

- ☒ continuation application.
- ☐ divisional application.
- ☐ continuation-in-part application. A Preliminary Amendment adding subject matter is attached.

1. Particulars of Prior Application

Application Serial No:	07/742,574
Filed on:	August 7, 1991
Title:	PHARMACEUTICAL COMPOSITIONS
Art Unit:	1502
Examiner:	W. Benston, Jr.
Prior Docket No.:	30484

CERTIFICATION UNDER 37 CFR 1.10

I hereby certify that this File Wrapper Continuing Application Transmittal Under 37 CFR 1.62 and the documents referred to as enclosed therewith are being deposited with the United States Postal Service on June 25, 1993, in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 utilizing the "Express Mail Post Office to Addressee" service of the United States Postal Service under Mailing Label No. IB916696088US.

Ed Putnam

3. **Declaration or Oath for Continuation-in-Part Application**

- ☐ Enclosed
- ☐ Not enclosed

4. **Amendments**

- ☒ Amend the specification by inserting before the first line the sentence:

"This is a Continuation of U.S. application Serial No. 07/742,574, filed August 7, 1991, in turn a Continuation of Serial No. 07/410,020 filed September 20, 1989, in turn a Continuation of Serial No. 07/133,520 filed December 16, 1987, now abandoned."

- ☐ Cancel claims ____ in the prior application before calculating the filing fee.
- ☐ A Preliminary Amendment is enclosed.
- ☒ Please enter the Amendment Under 37 CFR 1.116 previously filed in the prior application on May 10, 1993, but unentered.
- ☒ The filing fee is based upon entry of the foregoing amendment(s) (if any).

5. **Priority**

- ☒ Priority of application BA 86/30767 filed December 23, 1986; BA 86/30769 filed December 23, 1986; BA 86/30904 filed December 24, 1986; and BA 87/06684 filed March 20, 1987 filed in Great Britain is claimed under 35 USC 119.
  - ☐ The certified copy(ies) was(were) filed in prior U.S. application Serial No. _____.
  - ☒ The certified copy(ies) has(have) not been filed.

6. **Assignment**

- ☒ The prior application is assigned of record to Fisons plc, and has been recorded at Reel No. 4864, Frame No. 113.

7. **Small Entity Status**

- ☐ Verified statement(s) claiming small entity status is(are) attached.
- ☐ Small entity status has been established in the prior application and is still effective.

8. **Fee Calculation**

CLAIMS AS FILED - INCLUDING AMENDMENT(S) (IF ANY)						
			SMALL ENTITY		OTHER THAN A SMALL ENTITY	
	NO. FILED	NO. EXTRA	RATE	FEE	RATE	FEE
BASIC FEE				$355.00		$710.00
TOTAL	18 -20	= 0	X 11 =	$	X 22 =	$
INDEP.	3 - 3	= 0	X 37 =	$	X 74 =	$
☐ First Presentation of Multiple Dependent Claim			+ 115 =	$	+ 230 =	$
			Filing Fee:	$	OR	$710.00

9. **Method of Payment of Fees**

☒ Attached is a check in the amount of: $710.00

☐ Charge Deposit Account No. 13-2855 in the amount of: $_____
A copy of this Transmittal is enclosed.

10. **Deposit Account and Refund Authorization**

The Commissioner is hereby authorized to charge any deficiency in the amount enclosed or any additional fees which may be required during the pendency of this application under 37 CFR 1.16 or 37 CFR 1.17 to Deposit Account No. 13-2855. A copy of this Transmittal is enclosed.

Please refund any overpayment to Marshall, O'Toole, Gerstein, Murray & Borun at the address below.

Please direct all future communications to Basil P. Mann, at the address below.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN,
MURRAY & BORUN
6300 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606-6402
(312) 474-6300

By: _____
Basil P. Mann
Registration No. 18,464

June 25, 1993

Applicant(s): ANDREW R. CLARK ET AL.

Title: PHARMACEUTICAL COMPOSITIONS

Attorney Docket No. 31510

Mailing Certification for:

1. File Wrapper Continuing Application Transmittal Under 37 CFR 1.62

2. Fee for filing continuation application

Check No. 02394

"EXPRESS MAIL" mailing label No. ib91669608BUS

Date of Deposit: June 25, 1993

I hereby certify that this paper (or fee) is being deposited with the United States Postal Service "EXPRESS MAIL POST OFFICE TO ADDRESSEE" service under 37 C.F.R. §1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Ed Pietruski

Mail Room Date 6/25/93

MAY 12 1993

RECEIVED
MAY 2 1993
GROUP 1500

RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1502

#31/H
#38/J

PATENT APPLICATION

IN THE UNITED STATES PATENT
AND TRADEMARK OFFICE

Applicant:

ANDREW R. CLARK ET AL.

Serial No. ~~07/742,574~~ 08/082084

Filed: August 7, 1991

For:
PHARMACEUTICAL COMPOSITIONS

Group Art Unit: 1502

Examiner: W. Benston, Jr.

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231 on this date:

May 10, 1993

Basil P. Mann
Registration No. 18,464
Attorney for Applicant(s)

AMENDMENT "B" AFTER FINAL REJECTION

BOX AF
Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

In response to the Office Action of November 10, 1992, please amend the above-identified application as follows:

IN THE CLAIMS

Claim 7 (amended), line 3, after "aqueous" insert --pharmaceutical--.

Claim 18, line 10, after "aqueous" insert --pharmaceutical--.

090 PK 05/24/93 07742574 1 117 840.00 CK

Claim 21 (amended), line 3, after "aqueous" insert --pharmaceutical--.

Claim 21 (amended), last line, cancel "Ph" and insert --pH--.

REMARKS

The rejection of the claims under 35 U.S.C. §103 as unpatentable over Brown in view of Cox and GB '291 is respectfully traversed. The Examiner continues to allege that the disclosures of Brown and GB '291 are not equivalent in their teaching of pH ranges. As previously pointed out, the Examiner's contention is in error. Both Brown and GB '291 have exactly the same teaching, i.e., a pH range of 5.0-7.5 (Brown, col. 3, lines 18-19; GB '291, page 2, line 17). Applicants are unable to find in GB '291 a teaching of a pH range of 3.5 to 6.0, and respectfully request the Examiner to identify the section of the reference which does so.

The Examiner is also incorrect in his allegation that Brown teaches a pharmaceutical composition comprising an aqueous solution of nedocromil sodium. In reality, Brown teaches (col. 1, lines 40-41) ". . . a pharmaceutical formulation containing nedocromil sodium and a pharmaceutically acceptable liquefied gas aerosol propellant." This formulation is not an aqueous solution since water is not a liquefied gas aerosol propellant. As stated in the reference (col. 4, lines 41-47):

> The liquefied propellant medium, and indeed the total formulation is preferably such that the nedocromil sodium does

not dissolve therein to any substantial extent.

The liquefied propellant is preferably a gas at room temperature (20°C) and atmospheric pressure, i.e., it should have a boiling point below 20°C at atmospheric pressure (col. 4, lines 44-47). Clearly, the pharmaceutical formulations which are the object (col. 1, line 6) of the invention of Brown et al. are not aqueous solutions of nedocromil sodium.

The aqueous solution of nedocromil sodium which is disclosed by Brown et al. is used in the preparation of a solid form nedocromil sodium (col. 2, line 60 to col. 3, line 62), but this solution is not intended or disclose as suitable for administration to a patient.

In order to emphasize the distinction between the present invention in which the aqueous solution of nedocromil sodium is a pharmaceutical solution intended for use as such and the solution disclosed by Brown, the claims have been amended to specify that the solution is a pharmaceutical solution rather than one intended only as a starting material for production of another product.

The Examiner's argument that Brown teaches "pharmaceutical formulations," presumably referring to aqueous solutions of nedocromil sodium, is respectfully traversed. Contrary to the Examiner's allegation, the aqueous composition taught by Brown is not intended for administration to a patient, but rather for use in the preparation of solid nedocromil sodium for use in a pharmaceutical composition intended for administration.

It is not true as the Examiner implies, that every ingredient or component which is used to produce a pharmaceutical formulation is itself a pharmaceutical formulation. Brown's pharmaceutical formulations are compositions comprising solid nedocromil sodium and nonaqueous liquefied gas aerosol propellants, rather than aqueous solutions of nedocromil sodium. The Examiner's continued misdescription of Brown's product does not change this fact.

The "hard/soft capsules" containing solid materials disclosed by Cox are not equivalent to ampoules containing aqueous solutions. The Examiner has not demonstrated why or how the disclosure in Cox would suggest such ampoules, containing solutions and no solid materials, to one skilled in the art. Cox's capsules are intended for the packaging of powder compositions and not liquids, as shown by the reference to the capsules being filled to "less than about 80% by volume . . . with the powder composition" (col. 27, lines 15-18).

Taking the teachings and suggestions of the prior art as a whole, as they must be, there is no teaching or suggestion therein of making an ampoule of a carbon dioxide-permeable plastic material, filled with an aqueous solution of nedocromil sodium, and the Examiner has not demonstrated why such a product would be obvious to one skilled in the art in view of the teachings of the cited references.

The Examiner correctly states that it is not necessary for the prior art to suggest an invention literally; it is sufficient if the combined teachings and suggestions of the prior art would make a claimed invention obvious. It does not follow, however, that the distinctions and

deficiencies of the prior art can be ignored in demonstrating that the combined teachings of the art nevertheless suggest the claimed invention, unless the deficiencies are such that one skilled in the art would ignore them.

In the present case, the prior art does not deal with aqueous solutions of nedocromil sodium intended for administration as such, nor does the art teach or suggest filling plastic ampoules with such solutions. The capsules disclosed by Cox are filled with solid materials rather than aqueous solutions. The solutions disclosed by Brown are not intended for administration as such, but rather for the production of finely divided solid materials which are administered as aerosols. There is no suggestion in Brown to store aqueous solutions in capsules. These are serious and critical deficiencies in the prior art, and the Examiner has not alleged or demonstrated why one skilled in the art would ignore these differences and treat the prior art as suggesting ampoules filled with aqueous solutions of nedocromil sodium, when the teachings of the prior art are directly away from such products.

Although the Examiner states his "opinion" that the prior art teaches the present invention, his opinion is not based on the teachings of the references, as it must be. Similarly, although the Examiner states that it would be "prima facie obvious" to one skilled in the art to combine the teachings thereof, he has not demonstrated with the specificity which is necessary to support a proper rejection why it would have been obvious to do so.

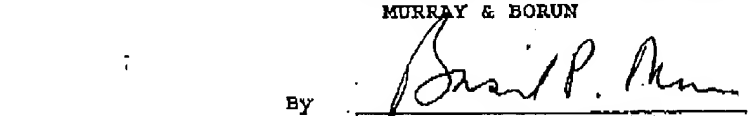
The Examiner alleges that the motivation for one skilled in the art to make the present invention "lies in

the composition of Brown who teaches said active ingredient in an aqueous solution in said weight/volume." The Examiner's allegation is only partially correct in that Brown teaches an aqueous solution, albeit not for administration or storage as such. Accordingly, there would be no motivation for one skilled in the art to encapsulate this aqueous solution in an ampoule or a capsule. The material which is encapsulated in accordance with Brown is a powder and not a solution.

The rejection is believed to be clearly deficient and improper. Reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN, MURRAY & BORUN

By 

Basil P. Mann (18,464)
A Member of the Firm
Attorneys for Applicant(s)
6300 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606
(312) 474-6300

Chicago, Illinois
May 10, 1993

PATENT APPLICATION SERIAL NO. 08/082804

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FEE RECORD SHEET

040 TD 07/16/93 08082804 1 101 710.00 CK 31510

PTO-1556
(5/87)

2. This request is filed by:

1. Full Name of Inventor	Family Name: Clark	First Given Name: Andrew	Second Given Name: Reginald
Residence & Citizenship	City: Loughborough	State or Foreign Country: England	Country of Citizenship: Great Britain
Post Office Address	Post Office Address: 32 Braddon Road	City: Loughborough	State & Zip Code/Country: England
2. Full Name of Inventor	Family Name: Wright	First Given Name: Paul	Second Given Name:
Residence & Citizenship	City: Bramcote	State or Foreign Country: England	Country of Citizenship: Great Britain
Post Office Address	Post Office Address: 9 Thornhill Close	City: Bramcote	State & Zip Code/Country: England
3. Full Name of Inventor	Family Name: Ratcliffe	First Given Name: Julia	Second Given Name: Helena
Residence & Citizenship	City: Alverstoke, Gosport	State or Foreign Country: England	Country of Citizenship: Great Britain
Post Office Address	Post Office Address: Flat 2, Crescent Road	City: Alverstoke, Gosport	State & Zip Code/Country: England

☐ This application is being filed by less than all the inventors named in the prior application. An accompanying statement requests deletion of the name(s) of the person(s) who are not inventors of the invention being claimed in this application.

07/742,574 08/07/91

Continuation of 07/410,020 09/20/89

07/742574

Request Form for File Wrapper Continuing Application under 37 CFR 1.62

#03 E. Jackson 8-2-91

DOCKET NUMBER	ANTICIPATED CLASSIFICATION OF THIS APPLICATION: CLASS	SUBCLASS	PRIOR APPLICATION: EXAMINER	ART UNIT
30484			L. Skaling	115

Address to:

Commissioner of Patents and Trademarks
Box FWC
Washington, D.C. 20231

This is a Request for filing a ☐ continuation-in-part ☒ continuation

☐ divisional application under 37 CFR 1.62 of prior application Serial No. 07/410,020, filed on Sept. 20, 1989; in turn a Cont. of U.S.S.N. 07/133,520 filed December 16, 1987, entitled: PHARMACEUTICAL COMPOSITIONS

501

by the following named inventor(s):

FULL NAME OF INVENTOR: FAMILY NAME	Clark	FIRST GIVEN NAME	Andrew
		SECOND GIVEN NAME	Reginald
RESIDENCE & CITIZENSHIP: CITY	Loughborough	STATE OR FOREIGN COUNTRY	England GB
		COUNTRY OF CITIZENSHIP	Great Britain
POST OFFICE ADDRESS: POST OFFICE ADDRESS	32 Braddon Road	CITY	Loughborough
		STATE & ZIP CODE/COUNTRY	England
FULL NAME OF INVENTOR: FAMILY NAME	Wright 402-94	FIRST GIVEN NAME	Paul
		SECOND GIVEN NAME	
RESIDENCE & CITIZENSHIP: CITY	Bramcote	STATE OR FOREIGN COUNTRY	England GB
		COUNTRY OF CITIZENSHIP	Great Britain
POST OFFICE ADDRESS: POST OFFICE ADDRESS	9 Thornhill Close	CITY	Bramcote
		STATE & ZIP CODE/COUNTRY	England
FULL NAME OF INVENTOR: FAMILY NAME	Ratcliffe 403-94	FIRST GIVEN NAME	Julia
		SECOND GIVEN NAME	Helena
RESIDENCE & CITIZENSHIP: CITY	Alverstoke, Gosport	STATE OR FOREIGN COUNTRY	England GB
		COUNTRY OF CITIZENSHIP	Great Britain
POST OFFICE ADDRESS: POST OFFICE ADDRESS	Flat 2, Crescent Rd.	CITY	Alverstoke, Gosport
		STATE & ZIP CODE/COUNTRY	England

The above identified prior application in which no payment of the issue fee, abandonment of, or termination of proceedings has occurred, is hereby expressly abandoned as of the filing date of this new application. Please use all the contents of the prior application file wrapper, including the drawings, as the basic papers for the new application. (note: 37 CFR 1.60 may be used for applications where the prior application is not to be abandoned.)

1. ☐ Enter the amendment previously filed on _____ under 37 CFR 1.116 but unentered, in the prior application.

2. ☒ A preliminary amendment is enclosed.

The filing fee is calculated on the basis of the claims existing in the prior application as amended at 1 and 2 above.

CLAIMS	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
	TOTAL CLAIMS	16 -20=	0	X$ 20 =	$ 0
	INDEPENDENT CLAIMS	3 -3=	0	X$ 60 =	0
	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+$ 200 =	
			BASIC FEE		+ 630.00
			Total of above Calculations =		
	Reduction by ½ for filing by small entity (Note 37 CFR 1.9, 1.27, 1.28). If applicable, verified statement must be attached.				-
			TOTAL =		$630.00

ATTORNEYS DOCKET NUMBER
30484

3. [X] The Commissioner is herby authorized to charge fees under 37 CFR 1.16 and 1.17 which may be required, or credit any overpayment to Deposit Account No. 13-2855.

4. [X] A check in the amount of $ 630.00 is enclosed.

5. [ ] A new oath or declaration is included since this application is a continuation-in-part which discloses and claims additional matter.

6. [X] Amend the specification by inserting before the first line the sentence:

This application is a [ ] continuation-in-part, [X] continuation, [ ] division, of application Serial No. 07/410,020, filed Sept. 20, 1989; in turn a Cont of U.S.S.N. 07/133,520 filed Dec. 16, 1987.

7. [ ] A verified statement claiming small entity status is enclosed. (necessary even if a statement was filed in the prior application)

8. [X] Priority of application Serial No. 86/30767 filed 12/23/86; 86/30769 filed 12/23/86, 86/30904 filed 12/24/86; & ~~87/06684 filed~~ filed on 3/20/87 in Great Britain is claimed under 35 U.S.C. 119.

9. [X] The prior application is assigned of record to Fisons plc

10. [X] The power of attorney in the prior application is to: Marshall, O'Toole, Gerstein, Murray & Bicknell

11. [ ] Also enclosed.

Address all future communications to: (May only be completed by applicant, or attorney or agent of record)

Basil P. Mann (Reg. No. 18,464)
MARSHALL, O'TOOLE, GERSTEIN, MURRAY & BICKNELL
Two First National Plaza
Suite 2100
Chicago, Illinois 60603

It is understood that secrecy under 35 U.S.C. 122 is hereby waived to the extent that if information or access is available to any one of the applications in the file wrapper of a 37 CFR 1.62 application, be it either this application or a pror application in the same file wrapper, the Patent and Trademark Office may provide similar information or access to all the other applications in the same file wrapper.

August 7, 1991
Date

Signature
Basil P. Mann (18,464)
[ ] inventor(s) [X] attorney or agent of record
[ ] assignee of complete interest [ ] filed under § 1.34(a)

Applicant(s): ANDREW REGINALD CLARK ET AL.

Title: PHARMACEUTICAL COMPOSITIONS

Attorney Docket No. 30484

Mailing Certification for: REQUEST FORM FOR FILE WRAPPER CONTINUING APPLICATION UNDER 37 CFR 1.62

"EXPRESS MAIL" mailing label No. B 82137733

Date of Deposit: August 7, 1991

I hereby certify that this paper (or fee) is being deposited with the United States Postal Service "EXPRESS MAIL POST OFFICE TO ADDRESSEE" service under 37 C.F.R. §1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Steven R. Zeliff

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Continuation Application of: ANDREW R. CLARK ET AL.

Based on Serial No. 07/410,020 filed September 20, 1989

Filed: Herewith

For: PHARMACEUTICAL COMPOSITIONS

Attorney Docket 30484

PRELIMINARY AMENDMENT

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Please amend the above-identified application as follows:

IN THE CLAIMS

Cancel claim 1.

Rewrite claim 7 as follows:

--7. (Amended) ~~A~~ [pharmaceutical composition comprising] an ampoule ~~container~~ of carbon dioxide permeable plastics material] filled with a unit dose of an aqueous pharmaceutical solution containing, as active ingredient, [the disodium salt of] 9-ethyl-6,9-dihydro-4,6-dioxo-10-propyl-4H-pyrano[3,2-g]quinoline-2,8-dicarboxylic acid or a pharmaceutically acceptable salt thereof, and sealed, the solution having a pH of 3.5 to 6.0.--

Cancel claim 9.

Rewrite claim 10 as follows:

--10. (Amended) A [pharmaceutical composition] ~~container~~ according to claim 7, wherein the concentration of active ingredient in the solution is from 0.1 to 5% w/v.--

Cancel claims 11, 12, 15, and 16.

Rewrite claim 17 as follows:

--17. (Amended) ~~A~~ [pharmaceutical composition] ~~container~~ according to claim 7, wherein the concentration of active ingredient in the solution is from 0.1 to 1.0% w/v.--

Add the following claims:

--18. A method of treatment of a disease selected from the group consisting of conjunctivitis, keratitis, "allergic eyes," adenovirus infections, corneal homograft rejection, anterior uveitis, nasal polyps, vasomotor rhinitis, allergic manifestations of the nasopharynx, reversible obstructive airways disease, Crohn's disease, distal colitis and proctitis, which method comprises administering to a patient suffering from such a condition the contents of ~~a container~~ of carbon dioxide permeable plastics material filled with a unit dose of an aqueous solution containing, as active ingredient, 9-ethyl-6,9-dihydro-4,6-dioxo-10-propyl-4H-pyrano(3,2-g)quinoline-2,8-dicarboxylic acid or a pharmaceutically acceptable salt thereof, and sealed, the solution having a pH of 3.5 to 6.0, as defined in claim 7.

19. A method according to claim 18 wherein the condition is reversible obstructive airways disease.

20. ~~A container~~ An ampoule according to claim 7 wherein the active ingredient is nedocromil sodium.

21. A ~~container according~~ to claim 7 which is ~~sterile-filled~~.

22. A container according to claim 7 which is a soft ampoule of carbon dioxide permeable plastics material.--

REMARKS

The rejection of claims 7, 9-12, and 17 under the doctrine of obviousness-type double patenting in view of claims 1-13 of U.S. Patent 4,868,192 is respectfully traversed in view of the amendment of the present claims to specify a container of carbon dioxide permeable plastics material containing an aqueous solution of the defined active ingredient in unit dosage form. The claims of the issued patent relate to compositions intended for topical administration to the skin, and would accordingly not suggest the container defined by the claims herein, wherein the container itself contributes to the stability in storage of the active ingredient contained therein as explained below.

The present invention is now restricted to its preferred form in which a unit dose of nedocromil sodium in aqueous solution is contained within a container of carbon dioxide permeable plastics material. In accordance with the invention now claimed, it has been found that the container improves the storage stability of the active ingredient, apparently by permitting carbon dioxide to permeate through

the walls of the container, thus reducing the pH of the solution, and improving the stability of the active ingredient. None of the references teaches that such a result is obtainable or how to achieve it.

The rejection of the claims as anticipated by Cairns, Dicker, Cox, or Fisons '722 is respectfully traversed. No single reference teaches a container containing an aqueous solution of nedocromil sodium as defined in the claims, and accordingly, none of the references can be considered to anticipate the present invention.

The rejection of certain claims as obvious under 35 U.S.C. §103 in view of Cairns or Dicker is respectfully traversed. While Cairns teaches the specific active ingredient now claimed, Dicker does not.

Further, while both references teach the use of the compounds in liquid carriers, neither of the references teaches water as a suitable carrier, and neither of them teaches a carbon dioxide permeable container as now claimed. Although the Examiner suggests that water would have been an obvious, even if undisclosed, liquid carrier for these compounds, it would not have been obvious that the use of a container in conjunction with an aqueous solution would improve the stability of the composition in storage.

The rejection of the claims as obvious over Cox is respectfully traversed for similar reasons. Cox does not teach the specific compound used in the present invention. Further, while Cox teaches the use of aqueous solutions of related materials in sealed containers and also recognizes the possibility of degradation in storage (column 27, lines 43-53), the reference does not teach or suggest that such

degradation could be inhibited by using a container made of a carbon dioxide permeable plastics material. Further, the disclosure of Cox relating to the use of containers does not teach or suggest that the material contained therein is an aqueous solution.

The rejection of the claims as obvious in view of Fisons '722 is also respectfully traversed. The reference does not teach use of aqueous solutions or the use of plastics containers nor does it suggest the beneficial results which are obtained through the use of such containers.

With respect to the rejections based on Corrado, Neale, or Schwaltz, there were filed in parent application Serial No. 07/410,020 certified copies of the priority documents on which the present application is based. These documents antedate the effective dates of these references, which are therefore not available for use in rejecting the present claims.

The Auty reference teaches only aqueous solutions of nedocromil sodium but does not supply any of the other deficiencies of the primary references with respect to the use of plastics containers to produce a unit dosage form.

With respect to double patenting in view of Patents 4,868,192 and 4,849,427, the Examiner has maintained the rejection of the composition claims. This rejection, however, is no longer deemed applicable in view of the amendment of the claims to require the defined container which is not covered by the reference patents.

The Examiner is respectfully requested to reconsider the conclusion that the Clark declaration is insufficient to overcome the rejection. The plastics

material used in the test reported by Mr. Clark was Esso Escorene LG 100AG which is permeable to carbon dioxide. Further, the requirement that the testing be conducted with a variety of other plastic materials is not believed to be appropriate. An unobvious advantage of the invention arises from the fact that storage in a carbon dioxide permeable plastics material produces unexpectedly beneficial results. Whether such results would also be achieved with other materials, also not taught by the prior art, is deemed to be not pertinent to the issue herein. Further, the requirement that it be established that the "change in pH is significant enough to effect an increase in stability over time" is also deemed to be improper. In the tests reported by Mr. Clark, the maximum decrease in pH over the storage period was 0.75 pH units, a decrease which is clearly not inconsequential. In view of the known improvement in stability of nedocromil sodium at lower pHs, the results are sufficient to demonstrate an unexpected superiority. Whether the change is "significant enough" as required by the Examiner depends on the particular circumstances which could not be assumed in a comparative test.

Reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN,
MURRAY & BICKNELL

By _____

Basil P. Mann (18,464)
A Member of the Firm
Attorneys for Applicant(s)
Two First National Plaza
Chicago, Illinois 60603
(312) 346-5750

Chicago, Illinois
Aug. 7, 1991